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A CYCLE OF MORPHINE ADDICTION

BIOLOGICAL AND PSYCHOLOGICAL STUDIES [1]

Part II: Psychological Investigations [2]

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CONTENTS

INTRODUCTION

The following study represents an effort to determine whether certain psychological and psychophysiological phenomena are changed with morphine or with morphine addiction in man. There are significant differences between man and the higher animals with reference to the effects of morphine, morphine addiction, withdrawal phenomena, and the desire for morphine following withdrawal of the drug (*1*). Spragg (*2*) reports that the chimpanzee shows no active desire for morphine 2 weeks after withdrawal. When considered in the light of the human addict's tendency to relapse to the use of morphine after months or years of abstinence, it becomes apparent that there are significant problems in the field of addiction which must be studied in the human.

Experiments have been conducted on the effects of single injections of morphine on such functions as simple reaction time (*3*, *4*, *5*), eye-hand coordination and memory (*6*), sensory thresholds and suggesti-

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[2] Part I: Biological Investigations, By Edwin G. Williams, Senior Surgeon, and Fred W. Oberst, Biological Chemist, was published in PUBLIC HEALTH REPORTS 61: 1-26. (Jan. 4, 1946). (The two parts of this article will be combined in one reprint.)

bility (*7*). A study of suggestibility in addicted and nonaddicted human subjects has been reported (*8*). No literature is available, however, on the effects of repeated injections of morphine upon these functions. An effort has been made in the present study to secure data bearing on the problem of mental efficiency in its relation to addiction, and for this purpose a wide sampling of tests has been employed, ranging from simple sensory and motor tests to complex tests of learning.

The effects of morphine and morphine addiction upon physiological reactions to psychological stimulation were undertaken because of the role which the emotions may play in the etiology of addiction. Inasmuch as the nature of the study required observations over a 2-year period, the plan of the experiment was handicapped by the fact that no studies have been reported in which measurements of emotional reactions have been made over such an extended period of time. The fact that emotional stimuli do not remain psychologically equivalent from one experimental period to the next raised the question as to the advisability of making frequent measurements during the course of the experiment with the hope of being able to correct for the effects of adaptation, or limiting the experimental trials to a single experiment before, during, and following addiction. The former plan was adopted, with the modification that different sets of word stimuli were used so that repetition of identical experiments would not occur until the lapse of at least 3 months. This allowed for a considerable number of experiments under various conditions.

The ideal subjects for study of this nature would, of course, be those who have had no former experience with opium or any of its derivatives. The possible social consequences of this kind of experimentation, however, rule against the use of subjects unfamiliar with morphine. The extent to which this condition restricts the significance of the findings is difficult to estimate. From the standpoint of the sociological problem of drug addiction, the use of post-addicts as subjects has some advantage over the use of subjects who have not demonstrated a strong desire for morphine.

APPARATUS

The following major pieces of apparatus were used in connection with this study.

The Darrow photopolygraph.—This apparatus gives a simultaneous recording of blood pressure changes (relative), pulse rate, respiration, skin resistance (conductance), tremor, voice- and hand-reaction time, and time of stimulus (*9*).

Apparatus for testing finger sensitivity to electric current.—This consisted of a thermal milliameter (range 0–2 milliamperes), two 45-volt

B batteries, voltmeter, two 200,000-ohm variable resistors, finger electrodes, and pan (15 inches long by 11 inches wide by 2½ inches deep) containing 2 liters of tap water for use as a physiologically inactive electrode. The finger electrode consisted of a round-headed brass machine screw (⅜-inch diameter) covered with chamois skin, which was attached to a lever having a spring for controlling pressure of the electrode on the finger. Direct current readings were taken. Skin resistance was calculated on the basis of known applied voltage and current as measured by the milliameter.

Apparatus for measuring steadiness.—This apparatus consisted of a long glass tube through which water flowed at the rate of 567 cc. per minute from a 10-gallon tank. The tube was held by the subject who was told to direct the stream of water into the small end of a funnel, the amount of water collected in a given time being taken as an indication of motor control. Diameter of the funnel opening was 7 millimeters. The subject stood at a distance of 1.5 meters from the funnel opening with the end of the tube held 8 cm. from the hole.

Apparatus for measuring tapping speed.—A Veeder counter was attached to hand rest which was constructed so as to immobilize all but the index finger which was left free for tapping.

TESTS

The following tests were used routinely throughout the study.

Word association tests.—These tests were used with the subject attached to the Darrow photopolygraph. Each set contained nine arbitrarily indifferent and nine disturbing words plus the introductory word "green." Each word, printed on a 5- x 8-inch card, was presented visually by means of a falling shutter arrangement which was electrically controlled. Twenty different sets of words were used. The subjects were requested to respond verbally with the first word coming to mind after presentation of the stimulus, at the same time depressing the right-hand tremograph key. The disturbing stimuli were divided into sex, crime, and drug words. Only one set of words was used at any experimental session.

Code learning test (Johnson).—Twenty-four different forms of this test were constructed, one of which is presented below:

Code

A B C D E F G H I J K L M N O P Q R S T U V W X Y Z
D Z H K P Q C A R V G O F Y E W X J L B M S I T U N

Test Material

Q T H O X E G C A Y P M K Z V W R B J M S F D U L I X O J T
M A G K U P B S W Q Z E I N Y V L E C F

Answer

X	B	A	E	T	P	C	H	D	U

In the sample shown above, the first series of letters has been placed in the squares as would be required of the subject. The subject was expected to transpose each of the series of letters into the proper squares. No attempt was made to equalize the difficulty of the forms of the test. It was found, however, that the monthly variability was less than that observed on any of the other measures. Score was the average time required to do one line of code.

Recognition of nonsense syllables.—Ten nonsense syllables were presented one at a time at 5-second intervals. Immediately after this initial presentation, a set of 20 syllables was presented, among which were the original 10. The subjects were requested to indicate which of these syllables were originally presented. The 20 cards were again presented 6 hours later with the same instructions, and this was called delayed recognition.

Delayed recognition.—Score was the number of syllables recognized. Twelve different forms of this test were used.

Oscillation (Scripture's blocks).—The subjects looked at the blocks for 2 minutes during which time they recorded each change in perspective on a Veeder counter.

Continuous subtraction.—The subjects were required to perform repeated subtraction of 13 from an initial number chosen from a range of 200 to 212. Time and errors were recorded.

PROCEDURE

The routine tests were arranged into four batteries, each battery being administered at predetermined periods throughout the study. With the exception of the first month, tests were given every other week. The intervening week was devoted to physiological investigations.

Battery X.—This battery included measures of finger sensitivity to electric current, steadiness, and code learning. About 50 minutes were required for its completion. The procedure in administration was as follows. The subject was first tested for sensitivity of the middle and ring fingers (right hand) to electric current. He sat in a chair with his back to the observer, his middle finger placed under the

electrode, with the right foot in the pan containing tap water. Starting at a very low level of intensity, brief electrical stimulations were administered at intervals of from 3 to 5 seconds, the intensity being increased at each succeeding stimulation until the subject consistently reported feeling the current. The intensity was then gradually decreased in steps of less than 0.05 milliamperes until the subject no longer reported the sensation. The median of three readings (midpoint between the appearance and disappearance of sensation) was taken as the sensitivity threshold. The middle and fourth fingers were tested alternately. Oral temperature was then taken (5 minutes) during the last minute of which pulse rate was counted. The code-learning test was administered, requiring approximately 5 minutes, immediately following which pulse and temperature were taken again. This battery of tests was administered at 8 a. m., 10 a. m., and 2 p. m. on Mondays, and at 9 a. m., 11 a. m., and 3 p. m. on Thursdays. A different code-learning test was used each time until the series of 24 tests was completed, after which the series was repeated.

Battery Y.—This battery consisted of a word-association test. The patient sat in a comfortable armchair with the fingers of each hand inserted in the tremograph. The Darrow electrodes were attached to the left wrist and palm, Redux paste being used on the wrists to eliminate resistance from that area. The blood-pressure cuff was attached to the left arm and the voice key was placed near the subject's mouth. In order to avoid discomfort, it was found necessary to maintain the cuff pressure at approximately 50 mm. of mercury. (In our experience the recommended pressure of one-third of the way from the diastolic to the systolic level is uncomfortable.) Tests were made at 8 or 9 a. m. (alternately) and at 2 or 3 p. m. (alternately) on Wednesday of every other week. A different association test was used at each sitting until the series was completed. This required approximately 4½ months, after which the words were repeated. The battery required about 45 minutes. Blood pressure was taken before and after each experiment.

Battery Z.—This battery included measurements of steadiness and tapping speed. In the steadiness tests two trials of 1½ minutes each were made with an intervening rest period of 3 minutes. Score was the amount of water directed into the bottle in 1½ minutes (average of the two trials). After completion of this test, tapping speed was studied. The subject was required to tap on a Veeder counter with his index finger as rapidly as possible for 10 seconds. Nine trials were made with a rest of 1½ minutes after each trial. Score was the median of the nine trials in terms of taps per 10 seconds. Pulse and temperature were taken before and immediately following the tapping speed experiment. This battery was administered at 8 a. m. and 2 p. m. on Tuesdays, and at 9 a. m. and 3 p. m. on Fridays.

Battery M.—This battery included tests of immediate and delayed recognition of nonsense syllables, oscillation, and continuous subtraction. Battery M was given on Fridays immediately following battery Z.

RESULTS

ROUTINE SENSORY, PSYCHOMOTOR, MEMORY, AND LEARNING TESTS

General Remarks

By the time morphine injections were begun the patients had become well-accustomed to the experimental routine. At no time did they appear to lose interest in the experiment, nor was the examiner able to notice any lack of cooperation during any phase of the study.

Attention has been directed (part 1) to the personality differences between the patients and to their antagonistic rivalry. This antagonism was less noticeable during the early stages of addiction, but reappeared after 3 or 4 weeks of morphine administration. During the single injection and early addiction phase it appeared that the morphine was producing feelings of elation in both subjects, more noticeable in M. It should be emphasized, however, that the effects of the drug upon gross behavior were much less than that generally reported for medium or large doses of alcohol. The elation was manifested by increased talkativeness, sociability, and a somewhat increased psychomotor activity, but these factors were seldom of sufficient magnitude to be noticed by anyone not familiar with the subjects' usual emotional tone.

As the injections were increased in frequency and amount, the patients apparently would be satisfied a few days after each increase in dosage, [3] but seldom was there a dosage level which maintained satisfaction for a period longer than 3 weeks. There was no indication from the spontaneous behavior of these patients that morphine had increased the feeling tone in the direction of pleasantness. Short periods of euphoria seemed to occur, but the general level of mood during the addiction period was in the direction of unpleasantness.

Finger Sensitivity

The sensitivity readings on the middle and ring fingers are shown in the two upper sections of figure 1. Each bar represents the monthly average (approximately 27 readings) expressed in terms of milliamperes. From November 1938 to February 1939, during which

[3] Dosage schedule: In order to establish norms and to observe their general behavior, the patients were studied for several months before morphine was administered. They were then given single doses (20 mg.) of morphine sulfate once weekly for 2 months. During the following 6 weeks the number of doses was increased, first to two and then to three injections per week, after which the drug was administered in single daily doses for 5 weeks. At the end of the daily single-dosage period, the drug was withheld for 3 days to determine whether physical dependence had developed. It was then given four times per day in increasing amounts, reaching 300 mg. per day by the seventeenth day, the highest dose being 4,440 mg. per day for 3 days just before the drug was discontinued.

period the effects of single injections were being studied, the bars have been separated to show the levels on morphine days. The figures below these months indicate the number of single injections which were being given each week during this period. It may be noted that

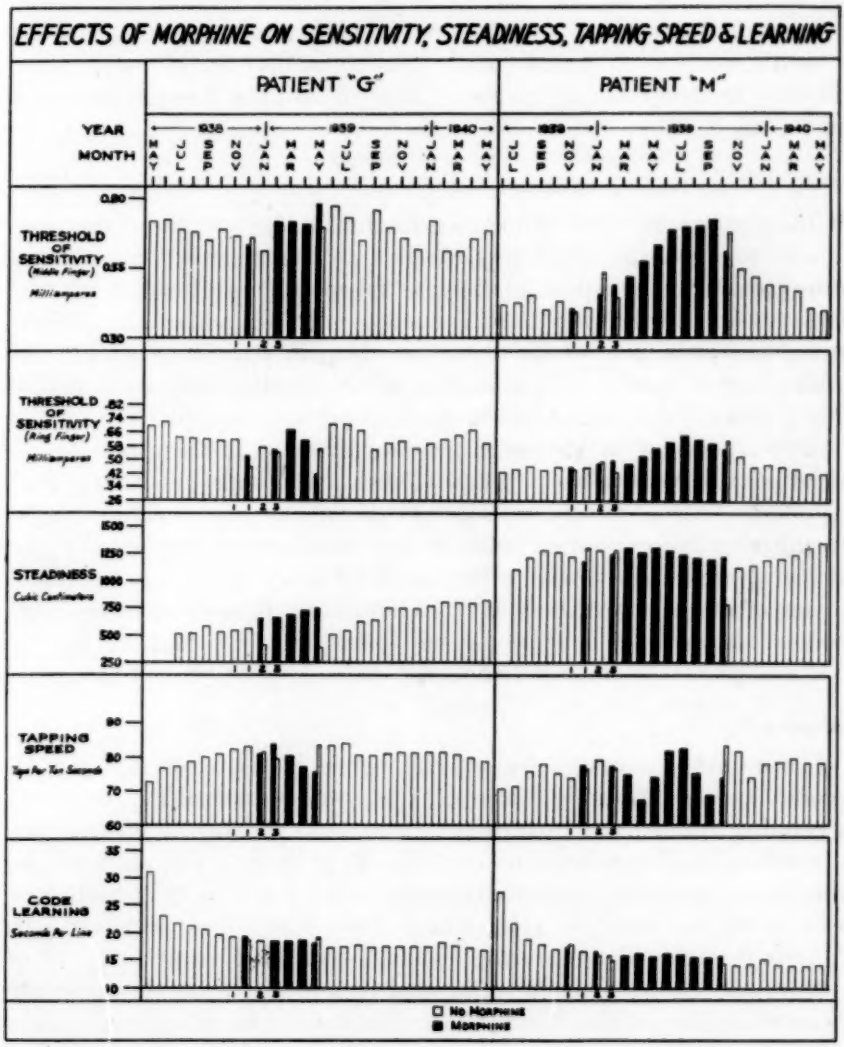

FIGURE 1.

G showed fluctuations in the monthly averages following morphine administration.

Finger sensitivity during the pre-addiction period for M was somewhat irregular and no significant effects of morphine were noted during the period of one injection per week. There was a rise in sensitivity when two injections were given per week, with the larger

rise occurring on the nonmorphine days. During the period in which three injections were given per week this relationship was reversed. As addiction proceeded, sensitivity became less, i. e., the threshold was increased. The highest threshold was in July for the ring finger and in September for the middle finger. Coefficients of correlation between the middle and ring fingers on this patient were 0.73 for the pre-addiction period, 0.88 for early addiction, 0.67 for late addiction, and 0.76 for the recovery period. After 6 months the original level was regained.

Steadiness

Changes in steadiness are shown in the middle section of figure 1. G, who was inferior to M with respect to this function, showed an improvement in steadiness following morphine injections, with the improvement continuing during each month of addiction. Withdrawal was associated with a marked drop in steadiness which was followed by a gradual rise to a plateau 5½ months after withdrawal. This plateau was slightly above the highest level reached during the addiction period. M showed a gradual increase in steadiness to an initial peak in September of 1938. During the single-injection period it appeared that steadiness was better on the nonmorphine days. During the latter part of addiction, motor control appeared to be somewhat diminished, with a sudden drop to an extremely low level 1 week following withdrawal. As recovery proceeded there was gradual improvement. There is no indication of a plateau having been reached at the end of 7 months.

Tapping Speed

The monthly averages for tapping speed in terms of taps per 10 seconds are also shown in figure 1. G showed a gradual improvement in tapping speed from 73 taps per 10 seconds in May to 83 taps per 10 seconds in December, the month just preceding the start of the morphine injections. After dropping to 81 the following month, a peak of 84 was reached, after which there was a gradual decline to 75 taps per 10 seconds during the last month of addiction. After withdrawal, the rate went to 83 and this level was maintained for 2½ months, after which the performance leveled off at approximately 80 taps per 10 seconds. At no time during 12 months following withdrawal did the performance drop to the level which obtained during the last 2 months of addiction.

M showed much more variability in this function than did G, especially during the addiction period. Two of the monthly averages in the addiction period were lower than any average obtained before or after addiction. Two other addiction averages were higher than the general level of performance. During the last addiction month

the level was 74 and there was an increase to 83 taps per 10 seconds 1 week after withdrawal of the drug. This figure was the highest obtained by the patient during the entire course of the experiment. There was a drop to 74 taps per 10 seconds 2½ months after withdrawal, after which the performance leveled off at approximately 79, with variations from 78 to 80 in the next 5 months.

Code Learning

Performance on the Johnson code-learning test is shown in figure 1. The values represented here are the monthly averages (approximately 27 experimental runs per month) in terms of seconds required to transpose one line of code. Although, in this test, neither of the subjects showed marked changes associated with morphine, G's improvement was arrested, and M showed a lower level of performance during the administration of morphine.

Continuous Subtraction

The performance of this test is presented in terms of monthly averages (four tests per month) in table 1. The monthly variability in performance was too great to allow for adequate interpretation of the averages obtained during the addiction period. The fact that M reached his peak performance 1 week after withdrawal of morphine may, however, be significant. G equaled his highest previous average during the withdrawal period, but this level was only slightly superior to the highest addiction average.

With reference to the average number of errors in continuous subtraction (table 1), the irregularities of the data obscure any trends which might exist. It may be noted, however, that if we omit the first month of the experiment for G, both patients showed the greatest number of errors during the last month of morphine.

Scripture's Block Oscillations

The number of alterations during the 2-minute period is presented as monthly averages (four readings per month) in table 1. No clear-cut trends can be noted for either subject.

Immediate and Delayed Recall of Nonsense Syllables

As may be noted from table 1, the changes in immediate and delayed recall are of insufficient magnitude in any particular direction to warrant conclusions with reference to the effects of morphine or morphine addiction on this function.

ANALYSIS OF PSYCHOPHYSIOLOGICAL DATA OBTAINED FROM WORD STIMULI

Introductory Remarks

The use of physiological functions as indices of psychological disturbances necessitates preliminary analysis to determine the psychological significance of the functions employed. It was not

TABLE 1.—*Results from tests in battery M*

Tests	Experimental conditions	1938						1939												1940				
		July	August	September	October	November	December	January	February	March	April	May	June	July	August	September	October	November	December	January	February	March	April	May
Continuous subtraction (seconds).	G																							
	Morphine							36		45	37	44												
	No morphine	82	57	57	60	50	40	43	40			36	45	35	48	37	34	31	31	30	28	41	28	33
	M																							
	Morphine						18		23	28	25	21	20	18	32	18	23							
	No morphine	25	38	35	30	29	21	23	22								16	28	22	20	25	22	18	18
Continuous subtraction (errors).	G																							
	Morphine							0.0		0.0	0.5	3.0												
	No morphine	4.0	1.6	1.3	1.5	1.5	2.0	0.0	0.0			1.0	1.0	0.0	1.5	0.5	0.0	1.0	1.7	1.0	1.5	2.0	2.0	1.0
	M																							
	Morphine						1.0		3.0	0.3	0.0	0.5	0.0	0.0	0.5	1.7	4.0							
	No morphine	3.0	0.0	0.5	1.3	0.5	0.0	0.0	0.0								2.0	1.0	0.5	1.0	0.0	1.0	1.5	3.0
Scripture block oscillations in 2 minutes.	G																							
	Morphine							53		72	58	67												
	No morphine	29	42	45	39	58	62	53	50			66	68	66	59	55	60	55	64	70	66	55	55	52
	M																							
	Morphine						46		42	42	39	39	44	41	47	35	45							
	No morphine	44	32	38	29	43	37	47	45								52	43	41	30	53	40	47	36
Immediate recall of nonsense syllables (syllables recognized).	G																							
	Morphine							19		18	17	15												
	No morphine	13	17	17	18	15	18	20	17			17	18	19	17	18	16	18	19	19	18	19	15	19
	M																							
	Morphine						18		15	17	17	17	17	19	18	19	14							
	No morphine	12	17	17	15	15	17	19	15								17	18	20	17	18	18	18	17
Delayed recall of nonsense syllables (syllables recognized).	G																							
	Morphine							15		15	11	13												
	No morphine	12	13	15	16	13	13	17	15			11	14	17	13	16	14	15	17	17	15	15	14	15
	M																							
	Morphine						13		13	14	16	15	18	16	15	16	16							
	No morphine	14	15	14	16	13	14	19	15								16	16	19	15	15	17	16	17

reasonable to assume that all or any of the functions measured by the Darrow photopolygraph could be accepted as valid indicators of psychological disturbance. Therefore it was necessary to determine the relative differences among these functions with reference to their discriminatory values.

The response difference between indifferent and disturbing words, or the response to a combination of indifferent and disturbing words, was taken as an indicator of the psychological significance of the physiological function under consideration. A lack of differential response does not necessarily indicate the inadequacy of a physiological variable as an indicator of psychological disturbance, since such a failure to differentiate may be caused by an inadequate choice of disturbing and nondisturbing words. In the case of positive and significant differences between responses to indifferent and disturbing words, however, it is reasonable to assume that the physiological function concerned is being affected by psychological factors, since only differences in meaning between the two sets of words could account logically for differences in physiological response.

Statistically significant differences (critical ratio of three or above) between the indifferent and disturbing words were found for conductance change, expiration time, time for five breaths as a percent of final rest, and voice-response time for both patients. Conductance recovery ratio, inspiration time, and hand-response time gave statistically significant differences between the indifferent and disturbing words for M, but not for G. Pulse rate, blood pressure, and amplitude of respiration did not show significant differences in either G or M.

Voice-Response Time

The effects of morphine on the voice-response time to the word stimuli (indifferent and disturbing words combined) are shown in figure 2. Each bar in this graph represents the average voice-response time for 1 month (usually four records, each record consisting of 19 stimuli). Records taken on those days on which morphine was administered are shown in solid color. The numbers under the bars represent the number of the injections which were being given per week during these periods. Recordings of this function, as well as that of hand response time, were not obtained until the beginning of December 1938. It may be noted from the graph that G showed an increase in time of response during the last 1½ months of addiction. Upon withdrawal there was a decrease in time of response, which was maintained below the average found during the last 1½ months of addiction.

In M, morphine appeared to increase the time of voice response during the single injection period. There was some decrease during the early stages of addiction. As addiction progressed, however, the

time of voice response increased. Upon withdrawal of the drug there was a significant drop and this level was consistently maintained during the remaining 7 months of the study.

Figure 3 shows that the differential response to disturbing and nondisturbing words was less under morphine than under comparable nonmorphine experiments.

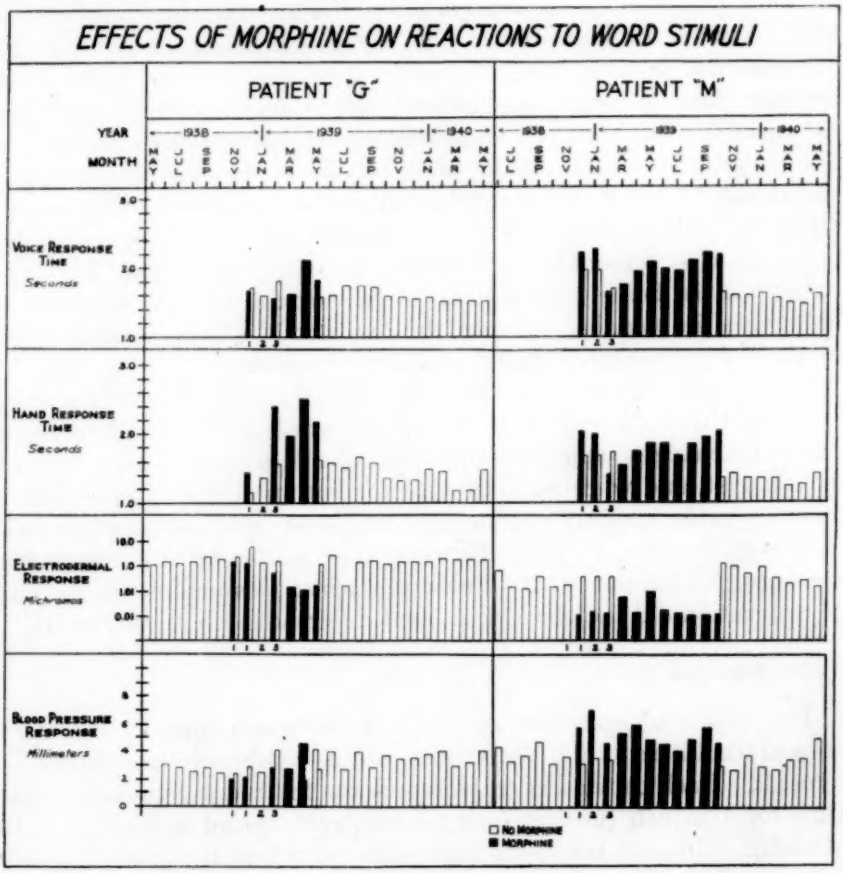

FIGURE 2.

Hand-Response Time

As mentioned in the procedure, the patients were requested to depress the right-hand Luria tremograph key when responding to the word stimuli. The effects of morphine and morphine addiction on this hand-response time are shown in figure 2. It may be noted that in both subjects the time of response was increased during addiction. M showed a reversal in the direction of effect during that period in which three injections per week were being administered, but, with the onset of addiction, he showed a gradual increase in the hand-response time, with a sharp decrease after withdrawal, and this was maintained for the remainder of the study.

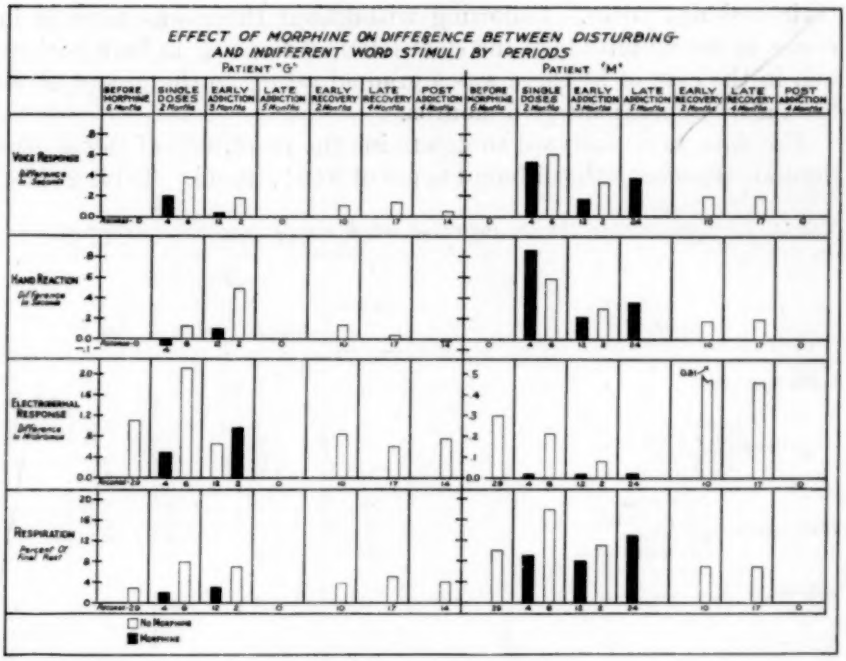

FIGURE 3.

The effects of morphine on differences in hand-response time between indifferent and disturbing word stimuli are shown in figure 3. M showed a greater difference between disturbing and nondisturbing word stimuli on days of morphine injection during the period of single doses. This was the only instance in which morphine differences were greater than nonmorphine differences. As stated above, this measure was not statistically significant for G, but the data are qualitatively similar to the usual finding that morphine reduces the disturbance value of stimuli.

The Electrodermal Response

The average amplitude of the electrodermal response to the word stimuli is shown in figure 2. The changes represented here are the monthly averages for all words combined. The amplitude of response is represented on the ordinate, and was derived by averaging the differences between the conductance level before each word stimulus and the level at the response peak. It may be noted that there was a reduction in the amplitude of the electrodermal response as morphine administration proceeded. This was gradual in G and abrupt in M. It may also be noted that the month of July 1939 showed an electrodermal change for G which is not in agreement with the general trend. During this month the patients were housed in a different section of the hospital, which was the only time they were quartered outside of

their assigned room. Following withdrawal there was marked increase in the amplitude of the electrodermal response in both patients and in the case of M there was a gradual return to the pre-addiction level after approximately 6 months.

The data were analyzed to determine the amplitude of the electrodermal response to the different types of word stimuli. Table 2 shows

TABLE 2.—*Conductance change following word simuli (expressed as micromhos)*

Period	Patient	Disturbing words			Indifferent
		Crime	Drugs	Sex	
Before morphine	G	3.39	3.76	4.30	3.23
	M	0.44	0.55	0.73	0.33
Single doses: Morphine	G	2.50	0.97	2.83	2.07
Single doses: No morphine	G	4.88	5.15	5.88	3.68
Single doses: Morphine	M	0.01	0.04	0.02	0.01
Single doses: No morphine	M	0.18	0.15	0.59	0.08
Early addiction: Morphine	G	3.89	0.46	1.38	1.79
Early addiction: No morphine	G	2.10	1.95	2.68	2.28
Early addiction: Morphine	M	0.01	0.04	0.10	0.06
Early addiction: No morphine	M	0.20	0.53	0.75	0.28
Late addiction	G				
	M	0.03	0.02	0.05	0.01
Early recovery	G	2.94	2.94	4.19	3.04
	M	1.22	1.03	2.10	0.48
Late recovery	G	4.37	3.11	4.19	2.24
	M	0.70	0.77	1.03	0.48
Post addiction	G	3.01	3.02	4.36	3.81
	M				

the average amplitude of the electrodermal response (average differences between conductance level before response and at the peak of response) classified into experimental periods. Sex words produced the largest electrodermal response. Following this in decreasing amplitude came the drug, crime, and indifferent words. In the case of G sex words failed to achieve first place on two occasions; once during morphine administration in the early addiction period, and once during the recovery period. Only on one occasion did the sex words fail to give the greatest response in M. This was on the morphine days during the single-injection period, at which time the drug words showed the greatest response, followed by sex, crime, and indifferent words. With the exception of crime words in G both subjects showed a marked increase in response following withdrawal of the drug.

The electrodermal response differences between disturbing and indifferent words were reduced following the administration of morphine. In the case of M, whose amplitude of electrodermal response was considerably less than that of G, the effect of morphine was to reduce the difference to almost zero. Following withdrawal of the drug there was a marked increase in the difference between the two types of stimuli, and the late recovery phase showed a return toward the original level.

Respiration

As previously mentioned, a statistically significant difference between indifferent and disturbing words was found for expiration time and time for five breaths as a percent of final rest. As the results of these two measures were very similar, only those for five breaths are shown in figure 3. It may be noted that wherever morphine records are compared with nonmorphine records in any particular period, the morphine records show smaller differences between the disturbing and nondisturbing words.

Blood Pressure Responses

The average blood pressure response to the word stimuli (all words combined) by monthly averages during the course of the experiment is shown in figure 2. During the period of single injections, morphine days are associated with a decreased response in G and an increased response in M. During the addiction period both patients gave a greater response than at any other time. This change was more marked in M, and is directly opposed to the change in electrodermal response.

This function did not show a statistically significant difference between disturbing and nondisturbing word stimuli.

INTERPRETATION OF RESULTS

The results indicate that the use of morphine is associated with a reduction in efficiency, although the effects are not of sufficient magnitude to constitute a serious disruption of general working efficiency. The voice- and hand-response times to word stimuli were increased, improvement in code learning was delayed, and speed of tapping was decreased during addiction in both patients. The greater variability observed for M with reference to tapping speed would indicate lower efficiency under conditions in which a constant level of performance of this type is required. There were no tests which clearly indicated any beneficial effects of the drug on efficiency. In tests of immediate and delayed recall, the highest scores were achieved under nonmorphine conditions. This was also true with reference to continuous subtraction. G seemed to show continuous improvement in steadiness under morphine, but his addiction level was surpassed under nonmorphine conditions after recovery from withdrawal.

The sudden improvement shown by both patients in tapping speed and continuous subtraction during the first 2 weeks following withdrawal of the drug probably reflects states of excitation during this period. The hyperactivity of M during the withdrawal phase was more pronounced than that observed in G. On continuous subtraction, M obtained his best score soon after withdrawal. The

significant decrease in motor control following withdrawal would be expected under conditions of increased excitation.

The results obtained by studying physiological responses to psychological stimuli indicate that morphine addiction is associated with an increase in hand-and voice-response time, a decrease in the amplitude of the electrodermal response, and an increase in the blood pressure response. Since these functions are highly integrated it is possible that the effects of addiction producing these results is a cortical depression. Andrews (*10*) interpreted some of the findings obtained by means of the electroencephalograph on the basis of cortical depression. This interpretation, however, does not definitely preclude the possibility of a secondary rather than a primary depression of the cortex.

As to the increased blood pressure response to word stimuli during addiction Himmelsbach (*11*) has shown that during addiction the blood pressure response is increased to cold pressor tests. He reported an opposite response to the cold stimulus following morphine in the nonaddicted individual, and in this study G showed a reduced response in the periods when morphine and nonmorphine days were compared.

None of the observed changes in the above experiments indicate the development of tolerance to the morphine effects even though one patient was kept on 300 mg. per day for over 2 months. Many of the functions were affected only slightly during the single-injection and early-addiction phases, with the direction of the effect becoming apparent only after addiction was well-established. This was true for such physiological functions as pulse rate and skin conductance level, as well as most of the psychological functions under discussion.

Probably the most significant finding of the present study is the reduction of the differential response between disturbing and nondisturbing words. The patients differed from each other with respect to certain physiological effects of morphine, such as respiration, temperature, pulse rate, and cortical potentials; and they differed considerably with respect to personality. Despite these differences the effect of morphine in both patients was to reduce the disturbance value of word stimuli. If this type of effect is extended to more realistic life situations, it would indicate that morphine is capable of ameliorating the disruptive effects of personal and social conflicts. Under such circumstances the reason for addiction to morphine and relapse to the use of the drug after various periods of abstinence becomes apparent.

SUMMARY

Psychological and psychophysiological studies were made on two post-addicts before, during, and following the development of tolerance to and dependence on morphine. Both patients were studied every other week over a 2-year period. The following measurements were taken: Johnson code learning, sensitivity to electric current, steadiness, tapping speed, continuous subtraction, Scripture's block oscilla-

tions, immediate and delayed recall of nonsense syllables, voice- and hand-response time and physiological reactions (blood pressure, pulse rate, skin conductance, and respiration) to word stimuli.

It was found that addiction to morphine was associated with a reduction in efficiency. The voice- and hand-response time to word stimuli was slowed; improvement in code learning was delayed; and speed of tapping was decreased during the latter stage of addiction in both patients. With the possible exception of steadiness in the case of G, there were no tests which indicated any beneficial effects of morphine addiction upon efficiency.

The amplitude of the electrodermal response to word stimuli was significantly reduced following the administration of morphine, whereas the blood pressure response to the same stimuli was increased. No satisfactory explanation of the opposite effects of the electrodermal response and blood pressure can be offered on the basis of evidence now available, but it was suggested that a release of lower centers from cortical inhibitory control may be involved.

The polygraphic data were subjected to statistical analysis to determine the extent to which the various functions gave a differential response to disturbing as compared with nondisturbing word stimuli. Statistically significant differences between indifferent and disturbing words were found for both patients with respect to electrodermal response, respiratory changes, and voice-response time. Morphine decreased the response difference between these two types of word stimuli. The suggestion was made that morphine may act to ameliorate the disturbing effects of emotional stress.

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THE RELEASE OF ANTIGEN FROM CERTAIN BACTERIA ON TREATMENT WITH ETHER [1]

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The release of a soluble antigen from typhus fever rickettsiae treated with ether was demonstrated by Topping and Shear (*1*), who shook saline suspensions of yolk sacs containing typhus rickettsiae with diethyl ether, and found that the resulting aqueous phase contained antigen which was not sedimented in the centrifuge along with the rickettsiae. This soluble antigen is complete in the sense that it not only reacts *in vitro* as a complement-fixation test antigen (*1*) and precipitin test antigen (*2*), but it also immunizes guinea pigs against the disease (*1*) and stimulates the formation of antibodies demonstrable in the complement-fixation test (*1*), neutralization test, and precipitin test (*3*).

Ether extraction of typhus-infected yolk sacs yields a much more potent vaccine (*4*), and the commercial production of typhus vaccine in this country utilizes the ether extraction process.

Similar release of antigen as a result of treatment with ether has been shown to occur with Rocky Mountain spotted fever rickettsiae (*Rickettsia rickettsii*) (*5*), *Proteus* OX19 (*3*), and *Pasteurella tularensis* (*6*). Larson (*6*) has also found that ether extraction of tularemia-infected yolk sacs produces a more potent vaccine, as tested in rats.

In this study a number of strains of bacteria have been examined to see if ether causes a release of antigen. Bacterial suspensions have been shaken with ether, and, after removal of the ether and after centrifugation, the supernatants have been examined for antigen by testing them by a precipitin test with rabbit serums prepared with untreated bacterial suspensions.

MATERIALS AND METHODS

Bacteria were cultivated on horse meat infusion agar slants. For the Brucella strains, 0.5 percent dextrose was added. For *Mycobacterium tuberculosis*, 5 percent glycerine agar was used. A suspension of *Pasteurella tularensis*, grown on glucose-cystine-blood agar, was obtained through the courtesy of Dr. Carl L. Larson.[2] Bacterial growths were gently rinsed from the slants and washed three times by centrifugation and resuspension in 0.85-percent saline containing 0.1 percent formalin.

Suspensions for the immunization of rabbits and for antigens in agglutination tests were prepared by diluting stock suspensions to match a 500-p. p. m. silica standard. Except for minor modification, rabbits were immunized by 1-ml. intravenous injections on the first,

[1] From the Division of Infectious Diseases, National Institute of Health.
[2] Division of Infectious Diseases, National Institute of Health.

second, third, eighth, ninth, and tenth days, and they were bled from the heart on the sixteenth day. The *Salmonella enteritidis* serum, however, was prepared by a longer course of less frequent and larger doses.

Agglutination tests were performed by mixing 0.2 ml. of the serum dilution with 0.2 ml. of the bacterial suspension. Tests were incubated at 37° C. for 4 hours and then left overnight at 4° C. before being read. Three of the bacterial suspensions (*M. tuberculosis*, *Bacillus anthracis*, and an unclassified gram-positive rod) were autoagglutinable, and their titers could not be accurately determined.

The ether treatment of the bacteria was accomplished as follows: Bacterial suspension, five times as concentrated as suspensions matching the 500-p. p. m. silica standard, was placed in a test tube, an approximately equal volume of diethyl ether (U. S. P. XII) was added, and the tube was stoppered and vigorously shaken for 5 seconds. The next morning the supernatant ether was pipetted off and discarded, and air was bubbled through the suspension to remove the dissolved ether. The bacterial bodies were sedimented in an angle centrifuge at 3,500–4,000 r. p. m. for 30 to 40 minutes. This amount of centrifugation was sufficient, except in the case of the tularemia and tuberculosis organisms which required more centrifugation. A control for each strain was treated the same way, except that no ether was added. The supernatants, which were clear in each case, were tested in a precipitin test for the presence of antigen.

Precipitin tests were carried out by mixing 0.2 ml. of dilutions of the supernatants with 0.2 ml. of 1:5 dilutions of the rabbit serums. After 4 hours of incubation in a 37° C. bath, the tests were kept at 4° C. until the next morning when they were read. Preparations were tested against serum prepared with homologous untreated bacterial suspensions, except in the case of the *Salmonella pullorum* antigens which were tested against *Salmonella gallinarum* serum. Serum controls and antigen controls (lowest dilution of antigen tested) were always included, and none showed precipitate.

RESULTS

Table 1 lists the results obtained. The readings, which indicate the amount of precipitate observed, show that the most pronounced reactions were seen with the antigens from *Proteus*, undulant fever, and tularemia organisms.

The precipitates in these tests resemble those seen with typhus antigens and their immune serums. They consist of floccules which sometimes coalesce in the tubes containing the greatest amounts of antigen, so that the sediment is resuspended with difficulty. Not much turbidity is seen in the supernatant even in the tubes near the end point.

TABLE 1.—*Liberation of antigen from bacteria as a result of ether treatment*

Organism	Precipitin tests on supernatants														Agglutination test titer of serum
	Ether-treated									Control					
	1	2	4	8	16	32	64	128	256	1	2	4	8	16	
Proteus OX19	[1] ++++	++++	++++	+++	+	0	0	0	0	0	−	0	−	0	>5,120.
Proteus OX2	++++	++++	+++	++	+	0	0	0	0	0	−	0	−	0	2,560.
Proteus OXK	++++	+++	+++	++	+	0	0	0	0	0	−	0	−	0	2,560.
Proteus HX19	−	++++	+++	++	++	+	0	0	0	−	0	0	0	0	640.
Proteus HX2	−	+++	++	+	0	0	0	0	0	−	0	0	0	0	640.
Proteus morgani	−	++++	+++	++	+	0	0	0	0	−	+	0	0	0	1,280.
Proteus americanus	−	±	0	0	0	0	0	0	0	−	0	0	0	0	320.
Brucella melitensis	++++	+++	++	+	0	0	0	0	0	±	±	0	0	0	2,560.
Brucella abortus	−	++++	++++	+++	++	+	0	0	0	0	0	0	0	0	1,280.
Brucella suis	−	++++	+++	++	+	0	0	0	0	0	0	0	0	0	5,120.
Pasteurella tularensis	++++	++++	++++	++++	++++	++	++	+	0	++	−	0	−	0	1,280.
Shigella paradysenteriae Flexner W	−	+	+	+	+	+	0	0	0	−	0	0	0	0	640.
Eberthella typhosus	−	+++	+++	++	++	+	0	0	0	−	0	0	0	0	640.
Salmonella enteritidis	±	−	±	−	0	−	0	0	0	0	−	0	−	0	1,280.
Salmonella paratyphosus B	−	+++	++	+	+	+	0	0	0	−	+	±	0	0	320.
Salmonella gallinarum	−	++	+	+	+	+	+	±	0	−	±	0	0	0	640.
Salmonella pullorum	−	+	+	+	+	+	+	0	0	−	+	+	+	0	*S. gallinarum* serum.
Mycobacterium tuberculosis	−	0	0	0	0	0	0	0	0	−	0	0	0	0	Auto-agglutinable.
Bacillus anthracis	++	−	+	−	0	−	0	−	0	+	−	0	−	0	Auto-agglutinable.
Bacillus subtilis	++	−	+	−	0	−	0	−	0	++	−	+	−	0	320.
Unindentified gram-positive rod	0	0	0	0	0	0	0	0	0	0	0	0	0	0	Auto-agglutinable.
Staphylococcus aureus	+	−	0	−	0	−	0	−	0	++	−	+	−	0	1,280.
Unindentified gram-positive coccus	+	0	0	0	0	0	0	0	0	0	0	0	0	0	160.

[1] Amounts of precipitate observed from greatest to least (++++ to +). ± indicates a questionable trace of precipitate, 0 no precipitate, and − that the antigen was not tested in that dilution.

On the other hand, the precipitates seen with the enteric organisms (Flexner, typhoid, and the salmonellas) were less voluminous and of a finer texture, and many tubes showed supernatant turbidity above a small amount of sediment.

The five gram-positive organisms tested showed little evidence of release of soluble antigen.

The presence or absence of flagellae did not appear to affect the result markedly. The H and O strains of *Proteus* X19 and X2 behaved similarly. In the organisms tested in the enteric group the nonflagellated organisms (Flexner, *gallinarum*, and *pullorum*) gave reactions not much different from the flagellated organisms.

Microscopic examination of bacterial suspensions exposed to ether gave little information. Some of the gram-negative rods showed a tendency to swell after exposure to ether, but there was little correlation between the estimated amount of swelling and the serological result. However, the tularemia organisms did show pronounced swelling, and in this respect they are similar to typhus fever rickettsiae which also show distinct swelling when treated with ether.

In table 2 are shown the results of centrifugation at a higher speed than that employed earlier. Ether-treated bacterial suspensions from which the ether had been removed were spun in an angle centrifuge at 3,600 r. p. m. for 1 hour. The supernatants were removed, and portions therefrom were centrifuged in an angle head at 14,000 r. p. m. for one-half hour.

The results show no change after high-speed centrifugation for the antigens prepared from *Proteus* OX19 or *Brucella melitensis*. However, the tularemia antigens show some drop in titer. It will be recalled that the tularemia organisms are different from the other organisms here observed in showing greater swelling on exposure to ether and also in requiring more centrifugation.

DISCUSSION

Some of the limitations of the method used for the demonstration of release of bacterial antigens should perhaps be emphasized. Only antigens soluble in saline solution would be detected, since those soluble in ether would be discarded, and those insoluble in ether or saline would be removed by centrifugation. Only antigens reactive in a precipitin test with rabbit serum for the whole organism would be found. Modifications of the test or use of a complement-fixation reaction might make possible detection of other antigens. If the rabbits had been immunized with the antigen preparations themselves, different results might have been had, since ether treatment may have changed the specificity of the antigen. Thus a negative finding may

TABLE 2.—*Results of centrifugation (14,000 r. p. m. for one-half hour) of antigen prepared by ether treatment*

Antigens from—	Precipitin tests														
	Before high-speed centrifugation—antigen dilution								After high-speed centrifugation—antigen dilution						
	1	2	4	8	16	32	64	128	1	2	4	8	16	32	64
Proteus OX19	++++	++++	++++	++++	+++	+	0	0	++++	++++	++++	++++	+++	+	0
Brucella melitensis	++++	++++	+++	++	0	0	0	0	++++	++++	+++	++	0	0	0
Pasteurella tularensis	++++	++++	++++	++++	++++	++	++	+	++++	++++	++++	++	++	+	0

have resulted from a lack of release of bacterial antigen or from a failure of the antigen released to react visibly.

The lethal effect of ether on bacteria was reported by Topley (7). It is interesting that the procedure for ether treatment adopted in the present study is almost identical with one used by Topley in 1915.

The relationship of the soluble antigens obtained here to such well-known preparations as those of Boivin and Mesrobeanu (*8*), of Raistrick and Topley (*9*), and of Morgan (*10*) is not as yet established.

SUMMARY

Ether treatment of certain bacteria resulted in the release of soluble antigen as demonstrated in a precipitin test with rabbit serum prepared against untreated organisms. The most abundant precipitates were seen with several strains of *Proteus*, with the three strains of *Brucella*, and with *Pasteurella tularensis*. Less abundant precipitates were seen with several other gram-negative bacilli. Little or no evidence of such soluble antigen was seen with several gram-positive organisms, although only a few strains were tested.

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PREVALENCE OF DISEASE

No health department, State or local, can effectively prevent or control disease without knowledge of when, where, and under what conditions cases are occuring

UNITED STATES

REPORTS FROM STATES FOR WEEK ENDED DECEMBER 22, 1945

Summary

A total of 68,497 cases of influenza was reported for the week, as compared with 148,688 for the preceding week, and 2,717 and 83,973, respectively, for the corresponding weeks of 1944 and 1943. Exclusive of the figures for Kentucky for both weeks, where 60 percent of the cases were reported last week (probably including some estimates), the figures are 61,681 for the current week and 59,325 last week.

Increases were reported in the Middle Atlantic, East North Central, South Atlantic, West South Central, and Pacific areas. The 13 States reporting more than 1,000 cases each for the week, aggregating 53,313 cases, or 89 percent of the total, are as follows (last week's figures in parentheses): *Increases*—Wisconsin 1,293 (388), Virginia 4,796 (4,691), West Virginia 7,219 (3,808), South Carolina 2,696 (2,659), Alabama 1,205 (649), Arkansas 2,021 (644), Oklahoma 1,170 (684), Texas 14,496 (11,259), Idaho 1,144 (279), Arizona 1,608 (1,163); *decreases*—North Dakota 1,134 (1,244), Kansas 7,715 (11,229), Kentucky 6,816 (89,363), Utah 9,434 (17,023).

The total from July to December 22 is 302,704, as compared with 28,879 and 215,986, respectively, for the corresponding periods of 1944 and 1943.

A total of 127 cases of meningococcus meningitis was reported as compared with 92 last week, 172 and 361, respectively, for the corresponding weeks of 1944 and 1943. The total to date is 7,837 as compared with 15,861 and 17,459, respectively, for the corresponding periods of 1944 and 1943, and a 5-year median of 3,587.

The incidence of poliomyelitis continued its downward seasonal trend—90 cases were reported as compared with 115 last week, 89 for the corresponding week last year, and a 5-year median of 48. The total for the year to date is 13,648 as compared with 19,196 and 12,358 for the corresponding periods of 1944 and 1943, and a 5-year median of 9,733.

An aggregate of 9,516 deaths from all causes was recorded for the week in 92 large cities of the United States, as compared with 9,313 last week, 8,576 for the corresponding week last year, and a 3-year (1942–44), average of 9,514 for the same cities. The cumulative total is 423,335, as compared with 423,147 for the corresponding period last year.

Telegraphic morbidity reports from State health officers for the week ended December 22, 1945, and comparison with corresponding week of 1944 and 5-year median

In these tables a zero indicates a definite report, while leaders imply that, although none was reported, cases may have occurred.

Division and State	Diphtheria			Influenza			Measles			Meningitis, meningococcus		
	Week ended—		Median 1940–44	Week ended—		Median 1940–44	Week ended—		Median 1940–44	Week ended—		Median 1940–44
	Dec. 22, 1945	Dec. 23, 1944		Dec. 22, 1945	Dec. 23, 1944		Dec. 22, 1945	Dec. 23, 1944		Dec. 22, 1945	Dec. 23, 1944	
NEW ENGLAND												
Maine	1	0	1	----	----	1	----	3	37	0	0	1
New Hampshire	1	0	0	----	----	----	2	1	4	0	0	0
Vermont	0	0	0	65	----	----	----	4	4	0	1	0
Massachusetts	5	5	4	----	----	----	124	52	294	2	4	4
Rhode Island	0	1	0	7	19	1	1	10	10	0	0	0
Connecticut	2	0	0	17	1	2	5	13	13	1	3	2
MIDDLE ATLANTIC												
New York	8	12	19	[1] 95	[1] 1	[1] 10	317	39	294	12	20	6
New Jersey	4	1	6	103	3	12	14	12	51	6	4	4
Pennsylvania	10	9	9	66	3	3	297	7	678	11	6	6
E. NORTH CENTRAL												
Ohio	38	10	10	191	3	12	8	11	46	3	6	2
Indiana	11	4	7	717	1	20	16	1	33	4	0	0
Illinois	4	1	8	585	2	11	184	21	64	10	9	0
Michigan [2]	16	19	8	6	4	2	219	14	59	5	11	1
Wisconsin	4	1	1	1, 293	18	31	31	13	164	3	5	3
W. NORTH CENTRAL												
Minnesota	7	16	4	----	----	1	4	3	29	2	6	1
Iowa	9	8	2	270	----	1	3	20	64	8	0	0
Missouri	6	6	5	46	----	3	53	4	13	1	1	1
North Dakota	1	16	3	1, 134	10	24	1	3	12	0	1	1
South Dakota	3	0	3	1	----	----	4	2	7	0	2	0
Nebraska	*0	0	1	514	11	5	4	3	8	0	0	0
Kansas	5	20	8	7, 715	2	15	56	7	25	0	2	1
SOUTH ATLANTIC												
Delaware	0	1	0	----	----	----	6	----	1	0	1	0
Maryland [2]	16	10	8	115	7	7	12	4	4	0	8	8
District of Columbia	1	0	0	6	----	3	2	2	3	0	1	1
Virginia	15	3	10	[1] 796	181	203	40	5	41	2	10	6
West Virginia	7	0	4	7, 219	17	18	2	14	14	3	1	1
North Carolina	37	6	9	----	7	10	31	18	31	0	3	2
South Carolina	7	12	6	2, 696	377	377	56	2	21	0	0	0
Georgia	8	16	7	298	33	71	3	4	18	0	2	2
Florida	6	7	7	12	----	9	6	----	2	0	5	1
E. SOUTH CENTRAL												
Kentucky	4	3	3	6, 816	3	18	120	1	12	2	4	1
Tennessee	20	12	11	394	16	52	3	7	29	7	4	3
Alabama	7	7	11	1, 205	86	143	----	3	20	4	2	2
Mississippi [2]	14	8	5	----	----	----	----	----	----	1	1	1
W. SOUTH CENTRAL												
Arkansas	18	6	6	2, 021	71	97	10	1	35	2	0	0
Louisiana	9	14	10	44	11	11	3	5	5	1	2	1
Oklahoma	6	13	8	1, 170	88	97	17	8	9	2	4	0
Texas	88	53	36	14, 496	1, 509	1, 320	49	44	44	7	17	2
MOUNTAIN												
Montana	1	1	0	943	1	15	8	1	26	1	1	0
Idaho	1	0	0	1, 144	2	2	30	4	3	1	0	0
Wyoming	0	0	0	----	15	66	15	1	10	1	1	0
Colorado	6	8	8	539	25	36	8	10	79	2	2	0
New Mexico	3	2	0	24	1	3	3	2	4	0	3	0
Arizona	9	0	0	1, 608	154	154	9	3	8	0	1	0
Utah [2]	0	0	0	9, 434	----	43	32	14	14	0	3	1
Nevada	0	0	0	----	----	----	31	----	----	0	0	0
PACIFIC												
Washington	3	17	2	----	----	4	148	40	40	3	3	2
Oregon	2	10	2	426	18	18	16	20	45	0	1	1
California	31	23	15	266	17	102	287	202	87	20	11	1
Total	454	361	281	68, 497	2, 717	2, 717	2, 290	658	4, 608	127	172	92
51 weeks	18, 200	13, 795	15, 236	377, 919	364, 402	293, 567	125, 960	601, 506	594, 435	7, 837	15, 861	3, 587

[1] New York City only.
[2] Period ended earlier than Saturday.

*Correction: Week ended Dec. 15, Nebraska, diphtheria, 2 cases (instead of 24).

Telegraphic morbidity reports from State health officers for the week ended December 22, 1945, and comparison with corresponding week of 1944 and 5-year median—Con.

Division and State	Poliomyelitis			Scarlet fever			Smallpox			Typhoid and paratyphoid fever [3]		
	Week ended—		Median 1940–44	Week ended—		Median 1940–44	Week ended—		Median 1940–44	Week ended—		Median 1940–44
	Dec. 23, 1945	Dec. 24, 1944		Dec. 23, 1945	Dec. 24, 1944		Dec. 23, 1945	Dec. 24, 1944		Dec. 23, 1945	Dec. 24, 1944	
NEW ENGLAND												
Maine	1	0	0	30	52	22	0	0	0	0	0	1
New Hampshire	0	0	0	0	8	8	0	0	0	0	0	0
Vermont	1	0	0	4	4	4	0	0	0	0	0	0
Massachusetts	3	5	1	111	283	238	0	0	0	2	0	0
Rhode Island	0	0	0	10	27	5	0	0	0	2	0	0
Connecticut	0	1	0	22	46	30	0	0	0	0	0	0
MIDDLE ATLANTIC												
New York	11	37	4	233	298	284	0	0	0	3	7	6
New Jersey	0	0	0	31	104	92	0	0	0	1	0	0
Pennsylvania	0	2	1	137	192	192	0	0	0	2	3	3
EAST NORTH CENTRAL												
Ohio	0	3	1	205	264	243	1	1	1	0	3	2
Indiana	1	0	0	55	60	68	0	0	0	0	0	1
Illinois	3	0	2	110	135	168	1	0	1	2	0	2
Michigan [2]	2	4	0	185	158	155	0	0	0	1	0	1
Wisconsin	4	2	1	106	122	141	0	0	0	0	1	0
WEST NORTH CENTRAL												
Minnesota	2	2	1	32	69	76	0	0	0	0	0	0
Iowa	5	0	0	42	36	56	1	0	0	0	0	0
Missouri	1	3	0	40	54	54	0	1	1	0	1	3
North Dakota	0	2	0	12	12	12	0	1	0	0	0	0
South Dakota	0	0	0	7	13	19	0	0	2	0	0	0
Nebraska	0	0	0	27	25	25	0	1	0	0	0	0
Kansas	2	0	0	56	100	82	0	1	0	0	0	0
SOUTH ATLANTIC												
Delaware	0	0	0	6	4	4	0	0	0	0	0	0
Maryland [2]	0	1	1	28	114	43	0	0	0	0	1	1
District of Columbia	1	0	0	12	37	16	0	0	0	0	0	0
Virginia	0	3	1	75	75	40	0	0	0	1	3	3
West Virginia	0	0	0	38	33	38	0	0	0	0	1	1
North Carolina	0	1	0	48	57	57	0	0	0	0	0	0
South Carolina	0	0	0	7	14	10	0	0	0	1	2	2
Georgia	4	0	0	15	27	23	0	0	0	2	1	1
Florida	3	1	0	5	8	6	0	0	0	5	3	2
EAST SOUTH CENTRAL												
Kentucky	0	1	0	30	32	43	0	0	0	0	2	2
Tennessee	0	0	0	29	58	58	0	0	0	2	0	1
Alabama	1	0	0	10	21	22	0	1	0	0	1	1
Mississippi [3]	4	0	0	30	22	10	0	0	0	0	1	1
WEST SOUTH CENTRAL												
Arkansas	0	1	1	17	8	5	0	0	0	1	0	1
Louisiana	0	1	1	12	10	8	0	0	0	0	0	3
Oklahoma	0	1	0	63	56	27	0	0	0	1	1	1
Texas	7	3	3	131	91	39	0	0	0	5	6	4
MOUNTAIN												
Montana	1	1	0	14	12	30	0	0	0	2	0	0
Idaho	0	0	0	6	51	7	0	2	0	0	0	0
Wyoming	0	2	0	1	18	11	0	0	0	0	0	0
Colorado	0	0	0	36	70	35	0	0	0	2	3	0
New Mexico	1	0	0	22	26	6	0	0	0	1	2	2
Arizona	1	0	0	16	15	5	0	0	0	0	0	1
Utah [2]	1	2	1	22	58	54	0	0	0	0	0	0
Nevada	0	0	0	0	1	1	0	0	0	0	0	0
PACIFIC												
Washington	4	1	1	12	110	44	0	0	0	0	1	1
Oregon	0	3	2	44	37	11	1	0	0	2	1	1
California	26	6	6	213	235	107	0	0	0	3	3	3
Total	90	89	48	2,397	3,362	2,776	4	8	19	41	47	49
51 weeks	13,648	19,196	9,733	170,178	186,557	137,454	343	385	801	4,814	5,349	6,652

[2] Period ended earlier than Saturday.
[3] Including paratyphoid fever reported separately, as follows: Massachusetts 2; Rhode Island 1; New York 2; New Jersey 1; Michigan 1; Georgia 2; Florida 5; Oklahoma 1; Texas 2; California 2.

Telegraphic morbidity reports from State health officers for the week ended December 22, 1945, and comparison with corresponding week of 1944 and 5-year median—Con.

Division and State	Whooping cough			Week ended Dec. 22, 1945							
	Week ended—		Median 1940–44	Dysentery			Encephalitis, infectious	Rocky Mt. spotted fever	Tularemia	Typhus fever, endemic	Undulant fever
	Dec. 22, 1945	Dec. 23, 1944		Amebic	Bacillary	Unspecified					
NEW ENGLAND											
Maine	44	54	26								
New Hampshire		2	5								
Vermont	19	10	18								2
Massachusetts	124	126	194	1	14						2
Rhode Island	24	24	24								
Connecticut	41	39	39		1						2
MIDDLE ATLANTIC											
New York	169	202	321	2	13			1			1
New Jersey	106	69	130								3
Pennsylvania	90	93	228						1		
EAST NORTH CENTRAL											
Ohio	52	92	133			1			2		
Indiana	13		13								
Illinois	38	47	89	3			1		4		
Michigan [3]	119	56	191	1	23						1
Wisconsin	70	87	128						1		4
WEST NORTH CENTRAL											
Minnesota	23	8	30	2					1		1
Iowa	3		18								
Missouri	9	7	11								1
North Dakota		11	11								
South Dakota	5	3	2								
Nebraska	5	6	3								
Kansas	17	32	39	1			1				2
SOUTH ATLANTIC											
Delaware	1	1	2							1	
Maryland [3]	24	53	53						2		
District of Columbia	6	7	9								
Virginia	46	37	59			15			3		1
West Virginia	8	18	14								
North Carolina	31	81	81			1			1		
South Carolina	86	23	29	5	2					3	
Georgia	6	5	10	1						22	
Florida	3	5	5	1					2	7	1
EAST SOUTH CENTRAL											
Kentucky	6	9	47						6		
Tennessee	8	4	19			1			1		2
Alabama	14	12	12							6	
Mississippi [3]										3	
WEST SOUTH CENTRAL											
Arkansas	1	12	22							2	1
Louisiana		4	4							7	0
Oklahoma	1	8	8								
Texas	147	108	128	9	303	45				21	7
MOUNTAIN											
Montana		9	9								
Idaho	17	12	12								
Wyoming		20	3								
Colorado	16	17	22	1	1						
New Mexico			9	1	1						
Arizona	9	4	4			17					
Utah [3]		8	11								
Nevada	4										
PACIFIC											
Washington	27	23	23								
Oregon	8	3	12								
California	90	90	137	4	7		1			5	6
Total	1,530	1,541	2,455	32	365	80	3	1	24	77	37
Same week, 1944	1,541			59	421	152	5	1	41	111	54
Average, 1942–44	1,772			33	298	71	6	[4] 1	28	[4] 77	
51 weeks: 1945	122,344			1,917	24,434	10,451	615	467	789	5,123	4,770
1944	90,040			1,857	24,295	9,046	625	454	674	5,265	3,771
Average, 1942–44	148,151		[4] 175,128	1,715	18,070	7,604	619	[4] 452	782	[4] 3,662	

[3] Period ended earlier than Saturday.
[4] 5-year median, 1940–44.

Anthrax: Massachusetts 1.

WEEKLY REPORTS FROM CITIES

City reports for week ended December 15, 1945

This table lists the reports from 87 cities of more than 10,000 population distributed throughout the United States, and represents a cross section of the current urban incidence of the diseases included in the table.

	Diphtheria cases	Encephalitis, infectious, cases	Influenza		Measles cases	Meningitis, meningococcus, cases	Pneumonia deaths	Poliomyelitis cases	Scarlet fever cases	Smallpox cases	Typhoid and paratyphoid fever cases	Whooping cough cases
			Cases	Deaths								
NEW ENGLAND												
Maine:												
Portland	1	0	------	0	1	0	5	1	1	0	0	7
New Hampshire:												
Concord	0	0	------	0	------	0	1	0	0	0	0	------
Vermont:												
Barre	0	0	------	0	------	0	0	0	0	0	0	------
Massachusetts:												
Boston	7	0	------	0	5	1	14	1	32	0	0	21
Fall River	0	0	------	0	------	0	1	0	2	0	0	6
Springfield	0	0	------	0	------	0	0	0	6	0	0	------
Worcester	0	0	------	0	4	0	8	1	10	0	0	8
Rhode Island:												
Providence	0	1	------	0	1	0	0	0	4	0	0	18
Connecticut:												
Bridgeport	0	0	------	0	------	0	1	0	1	0	0	------
Hartford	0	0	------	0	1	0	0	0	1	0	0	9
New Haven	0	0	1	1	2	0	3	0	0	0	0	10
MIDDLE ATLANTIC												
New York:												
Buffalo	0	0	3	0	1	0	6	0	13	0	0	17
New York	6	1	45	8	61	6	80	3	99	0	0	64
Rochester	0	0	------	0	1	3	1	0	5	0	0	7
Syracuse	0	0	------	2	144	0	2	0	15	0	0	2
New Jersey:												
Camden	0	0	------	1	1	1	1	0	2	0	0	5
Trenton	0	0	4	1	------	0	2	0	2	0	0	------
Pennsylvania:												
Philadelphia	5	0	54	4	64	2	26	0	46	0	0	35
Reading	0	0	------	1	1	0	0	0	0	0	0	15
EAST NORTH CENTRAL												
Ohio:												
Cincinnati	0	2	3	1	2	1	9	0	23	0	0	5
Cleveland	2	0	60	3	2	3	16	0	19	0	0	17
Columbus	12	0	------	0	------	0	5	0	14	0	0	1
Indiana:												
Fort Wayne	0	0	------	0	------	0	3	0	1	0	0	------
Indianapolis	3	0	------	0	------	1	9	0	5	0	0	6
South Bend	0	0	------	0	------	0	0	0	2	0	0	------
Terre Haute	0	0	------	0	------	0	7	0	0	0	0	------
Illinois:												
Chicago	0	0	13	7	167	4	48	2	45	0	0	42
Springfield	0	0	------	1	1	0	4	1	4	0	0	4
Michigan:												
Detroit	5	0	4	0	55	4	14	1	58	0	0	69
Flint	0	0	------	0	23	0	2	0	9	0	0	3
Grand Rapids	0	0	------	0	1	0	1	0	4	0	0	6
Wisconsin:												
Kenosha	0	0	------	0	------	0	0	0	1	0	0	------
Milwaukee	0	0	1	1	5	1	4	0	24	0	0	18
Racine	0	0	------	0	------	1	3	0	2	0	0	2
Superior	0	0	------	0	2	0	0	0	0	0	0	2
WEST NORTH CENTRAL												
Minnesota:												
Duluth	0	0	------	0	------	0	0	0	3	0	0	1
Minneapolis	3	0	------	0	2	0	5	0	10	0	0	4
St. Paul	1	1	------	2	1	1	1	0	5	0	0	1
Missouri:												
Kansas City	0	0	2	2	20	0	3	0	11	0	0	------
St. Joseph	0	0	----	0	15	0	0	0	1	0	0	------
St. Louis	3	0	22	4	3	2	11	7	14	0	0	1

City reports for week ended December 15, 1945—Continued

	Diphtheria cases	Encephalitis, infectious, cases	Influenza		Measles cases	Meningitis, meningococcus, cases	Pneumonia deaths	Poliomyelitis cases	Scarlet fever cases	Smallpox cases	Typhoid and paratyphoid fever cases	Whooping cough cases
			Cases	Deaths								
WEST NORTH CENTRAL—continued												
North Dakota:												
Fargo	0	0	------	0	1	0	0	0	1	0	0	------
Nebraska:												
Omaha	0	0	------	2	1	0	5	0	4	0	0	------
Kansas:												
Topeka	0	0	10	0	2	0	0	0	6	0	0	2
Wichita	1	0	1	0	2	0	6	0	5	0	0	------
SOUTH ATLANTIC												
Delaware:												
Wilmington	0	0	------	0	------	0	8	0	1	0	0	1
Maryland:												
Baltimore	11	0	26	2	3	1	7	0	21	0	1	28
Cumberland	0	0	1	0	------	0	2	0	0	0	0	------
Frederick	0	0	------	0	------	0	0	0	0	0	0	------
District of Columbia:												
Washington	0	0	22	0	2	0	10	0	13	0	0	5
Virginia:												
Lynchburg	0	0	799	0	------	0	1	0	5	0	0	9
Richmond	0	0	2	2	3	1	3	1	7	0	0	3
Roanoke	0	0	------	0	1	0	1	0	1	0	0	------
West Virginia:												
Charleston	0	0	------	0	------	0	0	0	0	0	0	------
Wheeling	0	0	1	0	------	0	1	0	0	0	0	------
North Carolina:												
Raleigh	0	0	------	0	------	0	2	0	1	0	0	------
Wilmington	4	0	------	0	------	0	2	0	4	0	0	2
Winston-Salem	0	0	------	0	------	0	1	0	6	0	0	------
South Carolina:												
Charleston	0	0	101	0	------	0	0	0	1	0	0	------
Georgia:												
Atlanta	0	0	82	0	------	0	10	2	3	0	0	------
Brunswick	0	0	------	0	1	0	1	0	4	0	0	------
Savannah	1	0	11	0	------	0	0	0	2	0	0	------
Florida:												
Tampa	1	0	------	0	------	0	2	0	3	0	0	------
EAST SOUTH CENTRAL												
Tennessee:												
Memphis	0	0	------	1	2	0	7	0	2	0	0	3
Nashville	0	0	------	3	6	0	5	0	2	0	0	------
Alabama:												
Birmingham	1	0	8	2	------	0	0	0	5	0	0	------
Mobile	0	0	------	0	------	0	2	0	0	0	0	------
WEST SOUTH CENTRAL												
Arkansas:												
Little Rock	0	0	------	0	------	0	2	0	0	0	0	------
Louisiana:												
New Orleans	4	0	6	2	------	1	5	4	11	0	1	1
Shreveport	0	0	------	0	------	0	4	0	2	0	0	------
Texas:												
Dallas	0	0	2	2	1	0	7	0	4	0	0	------
Galveston	0	0	------	0	------	0	0	0	0	0	0	------
Houston	7	0	------	0	------	1	3	0	8	0	1	------
San Antonio	1	0	15	2	------	0	8	1	0	0	0	------
MOUNTAIN												
Montana:												
Billings	0	0	------	0	------	0	1	0	1	0	0	------
Great Falls	0	0	------	0	------	0	0	0	0	0	0	------
Helena	0	0	------	0	------	0	0	0	0	0	0	------
Missoula	0	0	------	0	------	0	1	0	1	0	0	------
Idaho:												
Boise	0	0	------	0	------	0	0	0	0	0	0	------
Colorado:												
Pueblo	0	0	------	0	1	0	2	0	3	0	0	3
Utah:												
Salt Lake City	0	0	------	0	------	0	4	0	2	0	0	------

City reports for week ending December 15, 1945—Continued

	Diphtheria cases	Encephalitis, infectious, cases	Influenza		Measles cases	Meningitis, meningococcus, cases	Pneumonia deaths	Poliomyelitis cases	Scarlet fever cases	Smallpox cases	Typhoid and paratyphoid fever cases	Whooping cough cases
			Cases	Deaths								
PACIFIC												
Washington:												
Seattle	1	0	------	1	86	1	2	0	9	0	0	12
Spokane	0	0	1	0	6	0	2	0	5	0	0	6
Tacoma	0	0	------	0	39	0	0	0	2	0	0	8
California:												
Los Angeles	1	0	82	2	14	3	5	8	40	0	0	12
Sacramento	1	0	------	0	4	0	0	0	3	0	0	6
San Francisco	2	0	1	0	25	1	5	1	11	0	0	3
Total	84	5	1,383	60	786	40	423	34	693	0	3	510
Corresponding week, 1944	82	------	121	28	203	------	415	------	1,166	0	8	489
Average, 1940–44	73	------	1,698	[1]96	[2]1,223	------	[2]569	------	872	2	13	812

[1] 3-year average, 1942–44.
[2] 5-year median, 1940–44.

Dysentery, amebic.—Cases: New York, 3; Chicago, 1; Detroit, 1; Los Angeles, 1.
Dysentery, bacillary.—Cases: New York, 80; Charleston, S. C., 2; Memphis, 1; Los Angeles, 1.
Dysentery, unspecified.—Cases: Cincinnati, 1; Columbus, 1; San Antonio, 15.
Tularemia.—Cases: Cincinnati, 1; Chicago, 1; St. Louis, 2; Wichita, 1.
Typhus fever, endemic.—Cases: Atlanta, 2; Savannah, 2; Nashville, 1; Birmingham, 1; Little Rock, 2; New Orleans, 10 (Monthly report from Charity Hospital); Houston, 5; San Antonio, 1.

Rates (annual basis) per 100,000 population, by geographic groups, for the 87 cities in the preceding table (estimated population, 1943, 33,042,500)

	Diphtheria case rates	Encephalitis, infectious, case rates	Influenza		Measles case rates	Meningitis, meningococcus, case rates	Pneumonia death rates	Poliomyelitis case rates	Scarlet fever case rates	Smallpox case rates	Typhoid and paratyphoid fever case rates	Whooping cough case rates
			Case rates	Death rates								
New England	20.9	2.6	2.6	2.6	37	2.6	86.3	7.8	149	0.0	0.0	206
Middle Atlantic	5.6	0.5	53.9	8.6	139	6.1	60.0	1.5	93	0.0	0.0	74
East North Central	13.4	1.2	49.3	7.9	157	9.1	76.0	2.4	128	0.0	0.0	106
West North Central	15.9	2.0	69.6	19.9	94	6.0	61.7	13.9	119	0.0	0.0	18
South Atlantic	27.8	0.0	1,708.0	6.5	16	3.3	83.4	4.9	118	0.0	1.6	78
East South Central	5.9	0.0	47.2	35.4	47	0.0	82.6	0.0	53	0.0	0.0	18
West South Central	34.4	0.0	66.0	17.2	3	5.7	83.2	14.3	72	0.0	5.7	3
Mountain	0.0	0.0	0.0	0.0	16	0.0	130.2	0.0	114	0.0	0.0	49
Pacific	7.9	0.0	132.8	4.7	275	7.9	22.1	14.2	111	0.0	0.0	74
Total	13.3	0.8	218.8	9.5	124	6.3	66.9	5.4	110	0.0	0.5	81

* * *

DEATHS DURING WEEK ENDED DECEMBER 15, 1945

[From the Weekly Mortality Index, issued by the Bureau of the Census, Department of Commerce]

	Week ended Dec. 15, 1945	Corresponding week 1944
Data for 92 large cities of the United States:		
Total deaths	10,109	9,292
Average for 3 prior years	10,175	
Total deaths, first 50 weeks of year	445,641	445,311
Deaths under 1 year of age	632	604
Average for 3 prior years	646	
Deaths under 1 year of age, first 50 weeks of year	29,865	30,450
Data from industrial insurance companies:		
Policies in force	67,248,352	66,904,376
Number of death claims	12,464	12,878
Death claims per 1,000 policies in force, annual rate	9.7	10.1
Death claims per 1,000 policies, first 50 weeks of year, annual rate	10.0	10.1

FOREIGN REPORTS

BRITISH EAST AFRICA

Kenya—Relapsing fever.—A total of 1,552 cases of relapsing fever, with 376 deaths, has been reported in the coastal area of Kenya to November 30, 1945.[1]

CANADA

Provinces—Communicable diseases—Week ended November 24, 1945.—During the week ended November 24, 1945, cases of certain communicable diseases were reported by the Dominion Bureau of Statistics of Canada as follows:

Disease	Prince Edward Island	Nova Scotia	New Brunswick	Quebec	Ontario	Manitoba	Saskatchewan	Alberta	British Columbia	Total
Chickenpox		13		228	406	51	64	73	178	1,013
Diphtheria		3	3	31	23	9	2			71
German measles		6		3	14		1	11	10	45
Influenza		2			36	1				39
Measles		1	1	116	350		28	29	61	586
Meningitis, meningococcus				2	1			1	2	6
Mumps		2	1	166	85	16	11	87	49	417
Poliomyelitis					[1] 4			3		[1] 7
Scarlet fever		7	13	144	80	10	3	24	19	300
Tuberculosis (all forms)		15	15	93	59	63	2	4	55	306
Typhoid and paratyphoid fever				17	3				1	21
Undulant fever				1	3					4
Venereal diseases:										
Gonorrhea		22	30	104	180	56	48	50	93	583
Syphilis		17	10	153	114	11	3	22	47	377
Other forms				1						1
Whooping cough		3	1	131	43	3		5		186

[1] Includes 1 case, delayed report.

JAMAICA

Notifiable diseases—4 weeks ended October 20, 1945.—During the 4 weeks ended October 20, 1945, cases of certain notifiable diseases were reported in Kingston, Jamaica, and in the island outside of Kingston, as follows:

Disease	Kingston	Other localities	Disease	Kingston	Other localities
Cerebrospinal meningitis	2	1	Puerperal fever		3
Chickenpox	4	2	Scarlet fever	2	1
Diphtheria	12	9	Tuberculosis, respiratory	55	67
Dysentery, unspecified	12	9	Typhoid fever	16	204
Erysipelas	2	1	Typhus fever	5	1
Leprosy		3			

[1] See PUBLIC HEALTH REPORTS, Dec. 21, 1945, p. 1548.

SAINT HELENA

Poliomyelitis.—Poliomyelitis has been reported on the Island of Saint Helena, with 122 cases and 6 deaths up to December 9, 1945.

REPORTS OF CHOLERA, PLAGUE, SMALLPOX, TYPHUS FEVER, AND YELLOW FEVER RECEIVED DURING THE CURRENT WEEK

NOTE.—Except in cases of unusual incidence, only those places are included which had not previously reported any of the above-mentioned diseases, except yellow fever, during the current year. All reports of yellow fever are published currently.

A table showing the accumulated figures for these diseases for the year to date is published in the PUBLIC HEALTH REPORTS for the last Friday in each month.

Plague

Brazil.—During the month of August 1945, 3 cases of plague were reported in Ceara State, and 21 cases with 6 deaths were reported in Pernambuco State.

Smallpox

Mexico—Tuxpan.—During the month of October 1945, 20 cases of smallpox were reported in the port of Tuxpan.

Tunisia.—For the period November 11–20, 1945, 78 cases of smallpox were reported in Tunisia. Of these, 48 were in Nefta, among Algerian nomads. For the period November 21–30, 1945, 7 rural cases were reported.

Turkey.—For the week ended December 8, 1945, 2 cases of smallpox were reported in Turkey, 1 in the port of Seyhan, and 1 in the port of Ordu.

Typhus Fever

Mexico.—For the month of October 1945, 145 cases of typhus fever were reported in Mexico, including 31 cases in Mexico City and 19 in the airport of Monterrey.

Morocco (French).—For the period November 21–30, 1945, 103 cases of typhus fever were reported in French Morocco. Of these, 52 were reported in the region of Casablanca.

Turkey.—During the week ended December 8, 1945, 36 cases of typhus fever were reported in Turkey, including cases in ports as follows: Balikesir 5, Erzurum 2, Kocaeli 1, Istanbul 6, Izmir 6, Seyhan 5, Sinop 1, and Trabzon 1.

Yellow Fever

Colombia.—For the period October 5–10, 1945, 1 fatal case of yellow fever was reported in Los Gorros, Fonseca Municipality, Magdalena Department. For the period August 24–30, 1945, 1 fatal case was reported in Nogales, Bolivar Municipality, Santander de Norte Department.

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FEDERAL SECURITY AGENCY

UNITED STATES PUBLIC HEALTH SERVICE

THOMAS PARRAN, *Surgeon General*

DIVISION OF PUBLIC HEALTH METHODS

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